

YOUNG & THOMPSON

International Patent & Trademark Law

Established 1903

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1875-1936William H. Young
1902-1958Irvin S. Thompson
1903-1979

January 19, 2010

Examiner Mark Staples
Art Unit 1643
United States Patent and Trademark Office
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U.S. Application No. 10/547,669

Our Ref.: 2503-1170

Dear Examiner Staples,

Thank you for granting a telephonic interview for tomorrow, January 20, 2010 at 3:00 PM. Your time and consideration are greatly appreciated. I apologize for the delay in forwarding the data.

Please see the comments attached to this telefax, which includes the concordance correlation coefficient (ρ_c) for the previously presented data, and a new table that compares the sensitivity and specificity with the claimed and "new" primers. Also Applicant has provided remarks regarding the Shuber reference.

I look forward to discussing this case with you tomorrow.

Kind regards,

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January 19, 2010

Page 2

BUCK deals with equivalence among primers with regard to their use for the sequence analysis of those regions. The characterization of genomic DNA through sequencing methods is different from the quantification of genomic DNA molecules/fragments according to the present application. That is, the test of BUCK has a different objective than the claimed invention, i.e., BUCK is a Qualitative sequencing evaluation, whereas the claimed invention is Quantitative.

The possibility of reading the genomic DNA sequence is not directly correlated with that of quantifying the DNA molecules or determining their integrity.

It is impossible to make a direct comparison with the primers used in BUCK, especially if the above considerations about the DNA used for Buck's tests are taken into account. The different data obtained using the claimed primers and respectively the new primers, as reported in the reply (January 2009), confirm the importance of the primers used:

Tumor no.	FL-DNA (ng)	
	"Claimed" primers	"New" primers
1	34	33
2	41	9
3	19	12
4	42	12
5	10	10
6	9	3
7	35	3
8	21	8
9	96	6
10	77	11
<u>Healthy donor no.</u>		
1	9	6
2	13	9
3	13	7
4	14	13
6	4	13
6	15	2
7	25	12
8	17	4
9	0	2

Sample concordance correlation coefficient (p_c): 0.0456

January 19, 2010

Page 3

As can be seen from the above table and confirmed by sample concordance correlation coefficient (ρ_c), the two approaches based on different primers and using the same samples at the same time produce different values.

Taking into consideration these different values obtained, as shown in the table below, the test sensitivity and specificity are not the same when different primers are used:

Cut-off (ng)	Sensitivity (%)		Specificity (%)	
	Claimed	New	Claimed	New
10	90	80	30	40
15	80	30	70	70
20	70	10	80	100
25	60	10	80	100
30	60	10	90	100

As to SHUBER, Applicant has a published study comparative study (Neoplasia 6:536-540, 2004) where a method based on agarose gel (as described by SHUBER) is shown to be substantially different from fluorescence quantization in terms of accuracy in identifying neoplastic lesions. SHUBER erroneously states that various methodological approaches may determine equivalent results.